GLY CYS GLY LEU LEU HIS ASN TYR GLY VAL TYR THR LYS VAL SER ARG TYR LEU ASP TRP ILE HIS GLY HIS ILE ARG ASP LYS GLU ALA PRO GLN LYS SER TRP ALA PRO

wherein ALA is Alanine, ARG is Arginine, ASN is Asparagine, ASP is Aspartic Acid, CYS is Cysteine, GLN is Glutamine, GLU is Glutamic Acid, GLY is Glycine, HIS is Histidine, ILE is Isoleucine, LEU is Leucine, LYS is Lysine, MET is Methionine, PHE is Phenylalanine, PRO is Proline, SER is Serine, THR is Threonine, TRP is Tryptophan, TYR is Tyrosine, and VAL is Valine.

98. The constructed, recombinant DNA sequence of claim 97, which has been activated to remove amino acid residues 200-211 of human protein C, which are ASP THR GLU ASP GLN GLU ASP GLN VAL ASP PRO ARG.--

REMARKS

Entry of the foregoing, reexamination and reconsideration of applicants' application is respectfully requested in light of the following remarks.

Applicants note with appreciation the personal interview between Examiner Moore and applicants' representatives. During the interview, the outstanding rejection of claim 83 as being an improper recapture of claimed subject matter canceled in the application for the patent upon which the present reissue is based, was discussed. Applicants' representatives provided their opinion that claim 83 is not an improper recapture of the previously canceled subject matter.

The Examiner agreed to consider applicants' arguments in response to the Official Action. Alternative claims which would not be considered a recapture of subject matter were also suggested by the Examiner. Such claims are newly presented in the instant amendment.

The specification has been amended to correct an inadvertent typographical error. In the sequence listing, amino acid residue 264 was identified as "SRG". One skilled in the art would recognize that this is not a correct amino acid abbreviation and that it should instead be "ARG." No new matter is added by this amendment.

New claims 93 and 94 have been added as helpfully suggested by the Examiner. These claims are supported by the reissue application. Support for new claim 93 may be found at the very least in the sequences at pages 4-5 and 6-8. Support for claim 94 may be found at the very least at page 3, lines 1-3. New claims 95-97 have been added to be similar to claims 83, 93 and 94. These claims, however, do not recite the "active heavy chain" of protein C. Instead, these claims recite the heavy chain as including amino acids 200 to 211, which are present prior to activation. Support for these claims may be found at the very least at pages 4-5 and 6-7. New claim 98 is added to recite that the protein C has been activated to remove amino acid residues 200-211. Support for this claim may be found at the very least at page 3, lines 10-15, and at page 15, lines 42-46.

Appendix A contains a chart indicating the current status of all the claims of this application.

Applicants also note with appreciation the indication by the Examiner that claims 1-82

and 84-92 are allowable. The sole outstanding rejection is that of claim 83 under 35 U.S.C. §251 as being an allegedly improper recapture of claimed subject matter. This rejection is respectfully traversed.

Claim 83 allegedly includes "subject matter described by claims 101 and 102 presented at pages 3 and 4 of Applicants' Amendment A, Paper No. 5 filed March 23, 1987, in the prosecution of application Serial No. 06/699,967." Prior to being canceled, claims 101 and 102 stood rejected under 35 U.S.C. §103 as allegedly being unpatentable over a combination of references, including Foster et al (*see,* pages 3-5 of Paper No. 6, dated August 10, 1987).

Claims 101 and 102 recited:

> 101. A constructed, recombinant DNA sequence that comprises the coding sequence for the active heavy chain of human protein C, said active heavy chain having the amino acid residue sequence: ...
>
> 102. The DNA sequence of Claim [99] wherein the coding strand is: ...

The amino acid sequence and the DNA sequence for the heavy chain of human protein C are then recited in claims 101 and 102, respectively.

These claims were thus directed to the heavy chain of human protein C. As noted in the Official Action, these claims were rejected over a combination of references, which included Foster et al. Foster et al disclosed the heavy chain of human protein C, but only part of the coding sequence for the light chain of human protein C.

In contrast with claims 101 and 102, claim 83 recites:

> 83. The constructed, recombinant DNA sequence of claim 81, further comprising the

constructed recombinant DNA sequence that comprises the coding sequence for the heavy chain of human protein C, said heavy chain having the amino acid residue sequence:

LEU ILE ASP GLY LYS MET THR ARG ARG GLY ASP SER PRO TRP GLN VAL VAL LEU LEU ASP SER LYS LYS LYS LEU ALA CYS GLY ALA VAL LEU ILE HIS PRO SER TRP VAL LEU THR ALA ALA HIS CYS MET ASP GLU SER LYS LYS LEU LEU VAL ARG LEU GLY GLU TYR ASP LEU ARG ARG TRP GLU LYS TRP GLU LEU ASP LEU ASP ILE LYS GLU VAL PHE VAL HIS PRO ASN TYR SER LYS SER THR THR ASP ASN ASP ILE ALA LEU LEU HIS LEU ALA GLN PRO ALA THR LEU SER GLN THR ILE VAL PRO ILE CYS LEU PRO ASP SER GLY LEU ALA GLU ARG GLU LEU ASN GLN ALA GLY GLN GLU THR LEU VAL THR GLY TRP GLY TYR HIS SER SER ARG GLU LYS GLU ALA LYS ARG ASN ARG THR PHE VAL LEU ASN PHE ILE LYS ILE PRO VAL VAL PRO HIS ASN GLU CYS SER GLU VAL MET SER ASN MET VAL SER GLU ASN MET LEU CYS ALA GLY ILE LEU GLY ASP ARG GLN ASP ALA CYS GLU GLY ASP SER GLY GLY PRO MET VAL ALA SER PHE HIS GLY THR TRP PHE LEU VAL GLY LEU VAL SER TRP GLY GLU GLY CYS GLY LEU LEU HIS ASN TYR GLY VAL TYR THR LYS VAL SER ARG TYR LEU ASP TRP ILE HIS GLY HIS ILE ARG ASP LYS GLU ALA PRO GLN LYS SER TRP ALA PRO

wherein ALA is Alanine, ARG is Arginine, ASN is Asparagine, ASP is Aspartic Acid, CYS is Cysteine, GLN is Glutamine, GLU is Glutamic Acid, GLY is Glycine, HIS is Histidine, ILE is Isoleucine, LEU is Leucine, LYS is Lysine, MET is Methionine, PHE is Phenylalanine, PRO is Proline, SER is Serine, THR is Threonine, TRP is Tryptophan, TYR is Tyrosine, and VAL is Valine.

Claim 81 recites the "constructed, recombinant DNA sequence that comprises the coding sequence for the light chain of human protein C," and specifies the amino acid residue sequence. Claim 83 thus clearly includes the DNA sequence encoding ***both*** the light chain ***and*** the heavy chain of human protein C. By contrast, claims 101 and 102 recited the amino acid and DNA sequences, respectively, of ***only*** the heavy chain.

The MPEP §1412.02 states:

> Impermissible recapture occurs in a reissue where the claims in the reissue are of the same scope as, or are broader in scope than, claims deliberately canceled in an application to obtain a patent. Where such claims also include

> some narrowing limitation not present in the claims deliberately canceled in the application, the examiner must determine whether that narrowing limitation has a material aspect to it. If the narrowing limitation has a material aspect to it, then there is no recapture.

MPEP §1412.02 further states that "if the reissue claim is narrower in an aspect germane to a prior art rejection, and broader in an aspect unrelated to the rejection, the recapture rule does not bar the claim, ..."

As stated in In re Clement, 45 USPQ2d 1161 (Fed. Cir. 1997):

> If the scope of the reissue claim is the same as or broader than that of the canceled claim, then the patentee is clearly attempting to recapture surrendered subject matter and the reissue claim is, therefore, unallowable. *Ball, 729 F.2d at 1436, 221 U.S.P.Q. (BNA) at 295* ("The recapture rule bars the patentee from acquiring, through reissue, claims that are the same or of broader scope than those claims that were canceled from the original application.") (emphasis omitted); *Byers, 230 F.2d at 456, 109 U.S.P.Q. (BNA) at 56.* In contrast, a reissue claim narrower in scope escapes the recapture rule entirely. *Ball, 729 F.2d at 1436, 221 U.S.P.Q. (BNA) at 295.*

In the instant case, claim 83 is not of the "same scope as" or "broader in scope than" prior claims 101 and 102. Instead, in view of the requirement for the DNA sequences encoding *both* the light chain and the heavy chain of human protein C, claim 83 is narrower in scope than claims 101 and 102, which were directed to only the heavy chain of human protein C.

Moreover, the recitation of the DNA sequence encoding the light chain of human protein C "has a material aspect to it" and is "an aspect germane to a prior art rejection." This is evident by the fact that claim 83 was not rejected over Foster et al and in view of the fact that Foster et al discloses the heavy chain and only part of the light chain. As noted in the Official Action at

page 13, "the cDNA of Foster et al lacked the codons which specify '63 of the amino terminal amino acids of the light chain and all 42 of the amino acids for the pre-pro sequence.'" The recitation of the DNA encoding the amino acids of the light chain are thus material and claim 83 is narrower in an aspect germane to the prior art rejection of claims 101 and 102.

The Official Action states that "Claim 83 reaches both the subject matter which Applicants argued to be free of the prior art, a DNA encoding the entire amino acid sequence of the light chain of human Protein C, and, impermissibly, the subject matter which Applicants had relinquished to overcome a prior art rejection, a DNA encoding the complete heavy chain amino acid sequence of human Protein C." (Page 14). This statement shows that claim 83 is in fact narrower than claims 101 and 102. The fact that the claim reaches *both* the subject matter of the light chain and the heavy chain of human Protein C shows that the claim is in fact narrower than the canceled subject matter.

The Official Action states that "Claim 83 expands the subject matter embraced by claim 81 because it permits the previously-relinquished subject matter to be linked to that of claim 81 in a fashion whereby the additional codons can allow the transcription and translation of a Protein C heavy chain amino acid sequence independently of the amino acid sequence of the light chain." (Page 15). This position is in error. Whether or not the light chain and heavy chain are transcribed and translated independently, claim 83 recites a "constructed, recombinant DNA sequence" which comprises the coding sequence for the heavy chain and the coding sequence for the light chain of human protein C. The additional recitation of the coding

sequence for the heavy chain in claim 83 does not expand the subject matter of claim 81, but instead restricts it by specifying what additional DNA sequence must be present. Whether the light chain and the heavy chain are transcribed and translated independently and then joined together or whether they are transcribed and translated together is irrelevant. The claim requires the presence of the coding sequence of both the heavy and the light chains of human protein C. Requiring the presence of the light chain is sufficient to narrow the claim over prior claims 101 and 102 and remove the issue of recapture estoppel.

Claim 83 should thus not be barred under §251.

Withdrawal of the rejection of claim 83 is thus respectfully requested.

Applicants also note the Request for Interference Pursuant to 37 C.F.R. §1.607 filed on August 9, 1999, in this reissue application. Applicants renew their request that an interference be declared between the instant application and U.S. Patent Nos. 5,302,529 and 4,968,626 to Foster et al in accordance with the earlier request. The interfering subject matter of applicants' application and the Foster et al patents is directed to the cDNA encoding a full length human protein C polypeptide. Applicants' proposed Count is attached as Appendix B.

Further and favorable action in the form of an indication that the application is in condition for allowance, and declaration of an interference with U.S. Patent Nos. 5,302,529 and 4,968,626 to Foster et al are respectfully requested.

In the event that there are any questions relating to the response or the application in general, it is respectfully requested that the Examiner contact the undersigned attorney by telephone so that prosecution will be expedited.

Respectfully submitted,

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Date: April 14, 2000

APPENDIX A

CLAIM	STATUS
1	Pending in original form.
2	Pending in original form.
3	Pending in original form.
4	Pending in original form.
5	Pending in original form.
6	Pending in original form.
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89	Pending in original form.
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92	Pending in original form.
93	Newly added.
94	Newly added.

95	Newly added.
96	Newly added.
97	Newly added.
98	Newly added.

APPENDIX B

PROPOSED COUNT

A constructed DNA compound that comprises double-stranded deoxyribonucleic acid that encodes a polypeptide with human protein C activity, wherein the coding strand is:

$5'\text{-}R1_N\text{-}R_M$-GCC AAC TCC TTC CTG GAG GAG CTC CGT CAC AGC

AGC CTG GAG CGG GAG TGC ATA GAG GAG ATC TGT GAC TTC GAG

GAG GCC AAG GAA ATT TTC CAA AAT GTG GAT GAC ACA CTG GCC

TTC TGG TCC AAG CAC GTC GAC GGT GAC CAG TGC TTG GTC TTG

CCC TTG GAG CAC CCG TGC GCC AGC CTG TGC TGC GGG CAC GGC

ACG TGC ATC GAC GGC ATC GGC AGC TTC AGC TGC GAC TGC CGC

AGC GGC TGG GAG GGC CGC TTC TGC CAG CGC GAG GTG AGC TTC

CTC AAT TGC TCG CTG GAC AAC GGC GGC TGC ACG CAT TAC TGC

CTA GAG GAG GTG GGC TGG CGG CGC TGT AGC TGT GCG CCT GGC

TAC AAG CTG GGG GAC GAC CTC CTG CAG TGT CAC CCC GCA GTG

AAG TTC CCT TGT GGG AGG CCC TGG AAG CGG ATG GAG AAG AAG

CGC AGT CAC CTG AAA CGA GAC ACA GAA GAC CAA GAA GAC CAA

GTA GAT CCG CGG CTC ATT GAT GGG AAG ATG ACC AGG CGG GGA

GAC AGC CCC TGG CAG GTG GTC CTG CTG GAC TCA AAG AAG AAG

CTG GCC TGC GGG GCA GTG CTC ATC CAC CCC TCC TGG GTG CTG

ACA GCG GCC CAC TGC ATG GAT GAG TCC AAG AAG CTC CTT GTC

AGG CTT GGA GAG TAT GAC CTG CGG CGC TGG GAG AAG TGG GAG

CTG GAC CTG GAC ATC AAG GAG GTC TTC GTC CAC CCC AAC TAC

AGC AAG AGC ACC ACC GAC AAT GAC ATC GCA CTG CTG CAC CTG

GCC CAG CCC GCC ACC CTC TCG CAG ACC ATA GTG CCC ATC TGC

CTC CCG GAC AGC GGC CTT GCA GAG CGC GAG CTC AAT CAG GCC

GGC CAG GAG ACC CTC GTG ACG GGC TGG GGC TAC CAC AGC AGC

CGA GAG AAG GAG GCC AAG AGA AAC CGC ACC TTC GTC CTC AAC

TTC ATC AAG ATT CCC GTG GTC CCG CAC AAT GAG TGC AGC GAG

GTC ATG AGC AAC ATG GTG TCT GAG AAC ATG CTG TGT GCG GGC

ATC CTC GGG GAC CGG CAG GAT GCC TGC GAG GGC GAC AGT GGG

GGG CCC ATG GTC GCC TCC TTC CAC GGC ACC TGG TTC CTG GTG

GGC CTG GTG AGC TGG GGT GAG GGC TGT GGG CTC CTT CAC AAC

TAC GGC GTT TAC ACC AAA GTC AGC CGC TAC CTC GAC TGG ATC

CAT GGG CAC ATC AGA GAC AAG GAA GCC CCC CAG AAG AGC TGG

GCA CCT TAG-3'

wherein

A is deoxyadenyl,

G is deoxyguanyl,

C is deoxycytidyl,

T is thymidyl,

R is 5'-GCC CAC CAG GTG CTG CGG ATC CGC AAA CGT-3'

or 5'-CAC CAG GTG CTG CGG ATC CGC AAA CGT-3'

R^1 is

5'-ATG TGG CAG CTC ACA AGC CTC CTG CTG TTC GTG

GCC ACC TGG GGA ATT TCC GGC ACA CCA GCT CCT

CTT GAC TCA GTG TTC TCC AGC AGC GAG CGT-3'

or 5'-ATG TGG CAG CTC ACA AGC CTC CTG CTG TTC GTG

GCC ACC TGG GGA ATT TCC GGC ACA CCA GCT CCT

CTT GAC TCA GTG TTC TCC AGC AGC GAG CGT GCC-3'

M is 0 or 1, and

N is 0 or 1,

provided that when M is 0, N must necessarily also be 0 and that when

R is 5'-GCC CAC CAG GTG CTG CGG ATC CGC AAA CGT-3',

R^1 must necessarily be

5'-ATG TGG CAG CTC ACA AGC CTC CTG CTG TTC GTG

GCC ACC TGG GGA ATT TCC GGC ACA CCA GCT CCT

CTT GAC TCA GTG TTC TCC AGC AGC GAG CGT-3';

and that when

R is 5'-CAC CAG GTG CTG CGG ATC CGC AAA CGT-3',

R^1 must necessarily be

5'-ATG TGG CAG CTC ACA AGC CTC CTG CTG TTC GTG

GCC ACC TGG GGA ATT TCC GGC ACA CCA GCT CCT

CTT GAC TCA GTG TTC TCC AGC AGC GAG CGT GCC-3';

or

an isolated human DNA sequence which codes for a protein having substantially the same biological activity as human protein C;

or

a bacterial plasmid or bacteriophage transfer vector comprising cDNA coding for the amino acid sequence of FIG. 3, starting with alanine, number 1, and ending with proline, number 419, said cDNA sequence coding for human protein C.